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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,633	09/19/2003	Huimin Kong	NEB-210-US	8942

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,633	KONG ET AL.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *14-28,34-39 and 46-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,29-33,40-45,49 and 50* is/are rejected.

7)☒ Claim(s) *3-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/12/04;9/17/04;12/2/05; 12/19/05*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-45, 49 and 50; species A) in the reply filed on March 30, 2006 is acknowledged.

2. Claims 14-28, 34-39, 46-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species and inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 30, 2006.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on February 12, 2004 is in compliance with the provisions of 37 CFR 1.97, except for reference DQ, which does not have a place or date of publication. Accordingly, the information disclosure statement is being considered by the examiner with the exception of reference DQ.

5. The information disclosure statement (IDS) submitted on September 17, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

6. The information disclosure statement (IDS) submitted on December 12, 2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement

is being considered by the examiner. Reference BE was not considered, as the search report is not a publication.

7. The information disclosure statement (IDS) submitted on December 19, 2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, the references will not be printed, as they are duplicates of the IDS filed December 12, 2005.

Claim Objections

8. Claims 3-5 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 3 is not further limiting, as it contains the limitation "wherein the nucleic acid of step (a) is a single-stranded nucleic acid". This limitation is already present in step (a) of claim 1.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 31 recites the limitation "the thermostable helicase preparation" in lines 1, 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 31 depends, contains a limitation "a helicase preparation".

B) Claim 32 recites the limitation "the single stranded binding protein" in lines 1, 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 31 depends, does not contain a limitation "a single stranded binding protein".

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-10, 13, 29 and 40-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Sninsky et al. (U.S. patent No. 5,176,995).

Regarding claim 1, Sninsky et al. teach a method for exponentially and selectively amplifying a target nucleic acid, the method comprising :

(a) providing single strand templates of the target nucleic acid to be amplified (Sninsky et al. teach providing single stranded RNA to be amplified (col. 11, lines 13-20; col. 12, lines 50-64).);

(b) adding oligonucleotide primers for hybridizing to the templates of step (a) (Sninsky et al. teach converting mRNA to double-stranded DNA using reverse transcription, therefore they inherently teach providing oligonucleotide primers for hybridizing to the template (col. 11, lines 20-22). They further teach providing single-stranded target nucleic acid and using primers and agent of polymerization to synthesize the complementary strand (col. 12, lines 50-64), the agent of polymerization being a DNA polymerase (col. 13, lines 46-53).);

(c) synthesizing an extension product of the oligonucleotide primers which are complementary to the templates, by means of a DNA polymerase to form a duplex (Sninsky et al. teach converting mRNA to double-stranded DNA using reverse transcription, therefore they inherently teach synthesizing a DNNA duplex using DNA polymerase (col. 11, lines 20-22). They further teach providing single-stranded target nucleic acid and using primers and agent of polymerization to synthesize the complementary strand (col. 12, lines 50-64), the agent of polymerization being a DNA polymerase (col. 13, lines 46-53).);

(d) contacting the duplex of step (c) with a helicase preparation for unwinding the duplex (Sninsky et al. teach using helicase for unwinding the duplex (col. 14, lines 35-54); and

(e) repeating steps (b)-(d) to exponentially and selectively amplify the target nucleic acid (Sninsky et al. teach repeating the steps to exponentially amplify the target nucleic acid (col. 5, lines 61-68; col. 7,8; col. 9, lines 1-64; col. 14, lines 18-23; col. 15, lines 10-18).).

Regarding claim 2, Sninsky et al. teach isothermal amplification (col. 18, lines 40-49).

Regarding claims 3-5, Sninsky et al. teach single-stranded DNA and RNA (col. 11, lines 17-20).

Regarding claim 6, Sninsky et al. teach double-stranded nucleic acid denatured prior to step (a) (col. 12, lines 24-31).

Regarding claim 7, Sninsky et al. teach target nucleic acids with 107 bp (col. 17, lines 45-50) and 180 bp (col. 20, lines 51-62).

Regarding claim 8, Sninsky et al. teach a pair of oligonucleotide primers hybridizing to the 5' and 3' ends of nucleic acid to be amplified (col. 6, lines 61-68; col. 7, 8).

Regarding claim 9, Sninsky et al. teach a pair of oligonucleotide primers SK01 and SK02 for amplifying HIV DNA (col. 17, lines 45, 46). Primer SK01 is 17 bp long, and contains 9 G/C bases

and 8 A/T bases, whereas primer SK02 is also 17 bp long and contains 8 G/C bases and 9 A/T bases. Therefore the melting temperature of the SK01 primer is 52 °C, and the melting temperature of the SK02 primer is 50 °C, calculated based on the 4 °C melting temperature for the G/C base pairs and 2 °C melting temperature for the A/T base pairs. Therefore, since the amplification reaction with these primers was performed at room temperature, i.e., about 25 °C (col. 18, lines 40-49), the primers have melting temperatures about 25 °C higher than the reaction temperature.

Regarding claim 10, Sninsky et al. teach Klenow fragment of E. coli DNA polymerase (col. 13, lines 50, 51).

Regarding claim 13, Sninsky et al. teach a single helicase (col. 14, lines 46-49).

Regarding claim 29, Sninsky et al. teach an energy source for the helicase being ATP (col. 14, lines 49-51).

Regarding claims 40-42, Sninsky et al. teach performing the reactions at temperatures ranging from 50-105 °C or 40-50 °C, anticipating the limitations of about 20-75 °C, about 37 °C and about 60 °C, since Applicants did not define what range of temperatures corresponds to the term "about X °C".

Regarding claim 43, Sninsky et al. teach viral nucleic acids such as HIV, hepatitis A and B (col. 4, lines 34-40), therefore they teach pathogens.

13. Claims 1, 11-13, 31-33, 40-45, 49 and 50 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al. (U.S. Patent No. 6,977,148 B2).

Regarding claim 1, Dean et al. teach a method for exponentially and selectively amplifying a target nucleic acid, the method comprising :

(a) providing single strand templates of the target nucleic acid to be amplified (col. 8, lines 12-19; col. 34, lines 38-51);

(b) adding oligonucleotide primers for hybridizing to the templates of step (a) (col. 24, lines 63-67; col. 25, lines 1-20);

(c) synthesizing an extension product of the oligonucleotide primers which are complementary to the templates, by means of a DNA polymerase to form a duplex (col. 25, lines 1-20; col. 30, lines 35-48);

(d) contacting the duplex of step (c) with a helicase preparation for unwinding the duplex (col. 24, lines 17-36); and

(e) repeating steps (b)-(d) to exponentially and selectively amplify the target nucleic acid (col. 25, lines 53-60; col. 30, lines 49-64).

Regarding claim 11, Dean et al. teach polymerases lacking 5'-3' exonuclease activity (col. 23, lines 50-57).

Regarding claim 12, Dean et al. teach polymerase with strand displacement activity (col. 23, lines 50-57).

Regarding claim 13, Dean et al. teach a single helicase (col. 24, lines 17-36).

Regarding claims 31 and 32, Dean et al. teach a single strand binding proteins including phage T4 gene 32 protein (col. 24, lines 31—34).

Regarding claim 33, Dean et al. teach accessory proteins such as single-strand binding proteins (col. 24, lines 23-34).

Regarding claims 40-42, Dean et al. teach amplification at 30 °C (col. 36, line 40), therefore anticipating the limitations of about 20-75 °C, about 37 °C and about 60 °C, since Applicants did not define what range of temperatures corresponds to the term "about X °C".

Regarding claim 43, Dean et al. teach amplification of pathogenic nucleic acids (col. 5, lines 55-67; col. 6, lines 10-28).

Regarding claim 44, Dean et al. teach amplification of whole genomic DNA, therefore they inherently teach chromosomal DNA (col. 7, lines 49-51; col. 26, lines 50-55).

Regarding claim 45, Dean et al. teach determination of single nucleotide polymorphisms (col. 37, lines 5767; col. 38, lines 1-19).

Regarding claim 49, Dean et al. teach an assay for helicase, the assay comprising:

(a) preparing a helicase preparation comprising the helicase, an NTP or dNTP, a buffer, wherein the buffer has a pH in the range of about pH 6.0- 9.0, a concentration of NaCl or KCI in a concentration range of 0-200mM, and Tris-acetate or Tris-HCl and optionally one or more of a single stranded binding protein and an accessory protein (col. 24, lines 16-49; col. 36, lines 24-51);

(b) adding a target nucleic acid, oligonucleotide primers, four dNTPS and a DNA polymerase to the helicase preparation (col. 24, lines 16-49; col. 36, lines 24-51);

(c) incubating the mixture at a temperature between about 20 C and 75 C (col. 24, lines 36-49); and

(d) analyzing the DNA on an agarose gel to determine whether selective and exponential amplification has occurred (col. 36, lines 24-51).

Regarding claim 50, Dean et al. teach varying the temperature (col. 24, lines 36-49) and time of incubation (col. 38, lines 49-65).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sninsky et al. (U.S. patent No. 5,176,995).

A) Claim 30 is drawn to the concentration of ATP, dATP or dTTP in the range of about 0.1-50 mM. Sninsky et al. do not specifically teach such concentrations.

It would have been *prima facie* obvious to perform routine optimization using reagents, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection specific buffer component concentrations was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

16. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
6/11/06